TB/HIV

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Screening for Tuberculosis in Individuals with HIV Infection

A Clinical Guide for HIV Care Providers in Resource-limited Settings

International Center for AIDS Care and Treatment Programs
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About ICAP

The International Center for AIDS Care and Treatment Programs (ICAP), at Columbia University's Mailman School of Public Health in New York City, USA, supports HIV-related service delivery, training, and research, around the world. ICAP works with host countries and other organizations, principally in sub-Saharan Africa, to build capacity for family-focused HIV/AIDS prevention, care, and treatment programs. In support of HIV clinical programs, ICAP produces an array of resources for clinicians in resource-limited settings. ICAP programs are funded by a variety of sources, including United States government agencies and foundations.

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Figure 1. Glossary of Terms

Latent tuberculosis infection (LTBI):
LTBI results from exposure to and infection with *Mycobacterium tuberculosis*. People with LTBI do not exhibit any signs or symptoms and do not have TB disease, are not infectious, and cannot spread *Mycobacterium tuberculosis* to others. At least one third of the world's population has LTBI.

Tuberculosis disease (TB):
TB occurs most commonly when latent TB infection progresses or reactivates, and leads to the development of signs and symptoms of TB disease. People with TB develop symptoms such as cough, weight loss, loss of appetite, night sweats, fever, fatigue and chills. Those with TB affecting the lungs (pulmonary TB) can spread *Mycobacterium tuberculosis* to others through coughing and aerosolization of *Mycobacterium tuberculosis*. Many individuals with HIV infection develop more severe and complicated forms of TB, including extra-pulmonary TB (when TB disease affects a site in the body other than the lungs) and disseminated TB (when TB disease affects more than one site in the body, possibly including the lungs).

TB preventive therapy (Treatment of LTBI):
In the case of individual with latent TB infection, preventive therapy consists of antibiotic treatment to kill the latent *Mycobacterium tuberculosis* organisms and prevent the progression to TB disease. One of the most commonly used antibiotics for this purpose is isoniazid (INH) which must be taken for 6-9 months; this regimen is often called isoniazid preventive therapy or IPT.

Directly observed therapy (DOT):
DOT is observing a person with TB as they take their medications to treat TB. The observation is often done by a health care worker (although it is not necessary that the observer be a health care worker). Treatment for TB via DOT is recommended by many TB control programs and the WHO to ensure adherence and increase the likelihood of TB treatment completion and cure and reduce the development of multi-drug resistant TB.

DOTS: The World Health Organization's recommended framework for control of TB globally. It consists of five core elements which are:

a. Political commitment with increased and sustained financing
b. Case detection through quality-assured bacteriology
c. Standardized treatment with supervision and patient support
d. An effective drug supply and management system
e. Monitoring and evaluation system, and impact measurement

Provider-initiated counseling and testing:
Counseling and testing for HIV infection offered by health-care providers in the context of services, often via an opt-out approach.

Epidemiology terms used in this guide:
Sensitivity: The probability of a test detecting a disease among people who have it, or the proportion of people with a disease who test positive using the test.

Specificity: The probability of a test detecting no disease among people who do not have it, or the proportion of people without a disease who test negative using the test.

Positive predictive value (PPV): The percentage of people with a positive test result who actually have a disease (such as TB).

Negative predictive value (NPV): The percentage of people with a negative test result who do not have a disease (such as TB).

Introduction

More than one third of the global population is latently infected with *Mycobacterium tuberculosis*, the bacterium that causes TB disease: and for each second that passes, a new person becomes infected. Most people with LTBI never develop TB disease and do not transmit the infection to others. Healthy immune systems isolate *Mycobacterium tuberculosis* and prevent further multiplication and/or dissemination of the organism. Only five to ten percent of HIV-negative people with latent TB infection ever have progression of their LTBI and become ill with TB disease. People with TB disease of the lungs (pulmonary TB) can spread infection to others via coughing which introduces microscopic particles containing *Mycobacterium tuberculosis* into the air. Others then breathe in these infectious particles and become infected. Each individual with TB disease will infect an average of 10 to 15 others if they go undiagnosed and untreated and the cycle of transmission continues. In 2004, there were 8.9 million new cases of TB and 1.7 million deaths due to TB.

Tuberculosis is a much more serious condition for persons with HIV infection. HIV attacks the immune system which is critical for preventing progression of LTBI to TB disease and in helping control disease once it develops. When people have both LTBI and HIV infection, their risk of progression form LTBI to TB is increased 50-100 fold. People with HIV infection are more likely to have more severe forms of TB including disseminated and extra-pulmonary TB. As a result, TB is the leading cause of mortality in HIV-infected people, with up to one in three dying from tuberculosis. Twelve million people across the globe are co-infected with both HIV and TB. TB is especially problematic in sub-Saharan Africa. Africa has the highest number of both TB cases (more than 400 per 100,000 population per year) and HIV infections (24.5 million people living with HIV in Africa by the end of 2005), with two thirds of TB patients co-infected with HIV.

There is effective treatment for both prevention of progression of LTBI and cure of TB disease. Early diagnosis and treatment of TB disease can improve outcomes and decrease the spread of *Mycobacterium tuberculosis* in households, workplaces and health care settings. The most widely recommended strategy for TB control is the World Health Organization (WHO) DOTS framework, which includes Directly Observed Therapy (DOT) for TB. When patients follow DOT correctly, the cure rate for TB is 90 percent. Antiretroviral therapy (ART) is an important component of the management of TB/HIV co-infection. Many HIV-infected patients with TB disease qualify for ART and HIV-infected patients living in high TB burden areas who are started on ART have a decreased risk of developing TB disease.

Figure 2. Rationale for TB screening questionnaires

In a recent study in Cape Town, 129 patients with advanced HIV disease were screened for TB using a questionnaire that inquired about weight loss, coughing, night sweats and fever. After screening, thorough evaluations were performed in all patients including sputum smears, cultures and chest radiographs to look for evidence of TB disease. Using a positive culture for *Mycobacterium tuberculosis* as the gold standard for diagnosis of TB, the study found active TB in 11 of the 129 patients, or 8.5 percent. Researchers determined that when patients had two or more of the symptoms included in the questionnaire (including measured weight loss), the questionnaire had a sensitivity of 100 percent, a specificity of 88.1 percent, a positive predictive value of 44 percent, and a negative predictive value of 100 percent for determining whether or not someone who screened positive would have TB. (Mohammed et al. 2004).

Another study took place in Free State Province, South Africa and included 899 HIV-positive gold miners attending a preventive therapy clinic. Nurses administered a screening questionnaire that included questions regarding new or worsening cough, new or worsening sputum production, haemoptysis, night sweats, fever and self-reported weight loss. In addition, medical staff assessed weight loss from the time of first employment. Chest radiographs were performed and compared to any prior chest radiographs. Sputum specimens were collected for smear and culture, and blood was taken to determine CD4 cell count. Researchers found that the symptoms with the greatest sensitivity and negative predictive value (NPV) were night sweats, new or worsening cough and weight loss. The inclusion of chest radiographs in the screening process in this study significantly increased the sensitivity and NPV of TB screening. Active TB was identified in 44 miners, or 4.9 percent, and was most common in those with a lower CD4 count. (Day et al. 2006)

Results of these two studies are summarized in Table 1.

Table 1. Comparison of two South African studies evaluating methods for screening for TB in HIV-infected individuals

	n	Population	TB Prevalence	Conclusion on Best TB Screening Process
Cape Town	129	HIV-infected out-patients, WHO stage 3-4	11/129 (8.5%) 10 culture positive	Symptoms and weight loss
Free State	899	Mineworkers, WHO stage 1-4 (46% Stage 1)	44/899 (4.9%) 35 culture positive	Chest radiograph, symptoms and weight loss

TB Screening in Resource-Limited Settings

An essential strategy for decreasing the burden of tuberculosis and preventing its spread in people with HIV is integration of TB and HIV activities, care and treatment. This includes TB screening and active case finding in the clinical settings where people with HIV infection receive their care.

All patients with HIV infection should undergo routine screening to determine whether they may have tuberculosis. Screening for TB disease can be done with the administration of a simple questionnaire asking about symptoms related to possible TB disease. If patients screen negative for symptoms consistent with TB disease (i.e. answer no to all symptoms), health care providers can administer the screening questionnaire again in three to six months' time. If they answer positively to any of the questions, then, this suggests that the patient may have TB disease. This patient should be considered a TB suspect and an evaluation for TB disease should begin. This evaluation should include at least three sputum samples for smear microscopy to look for acid-fast bacilli which would be consistent with TB disease. The evaluation could also include, when available, a chest radiograph to aid in the diagnosis.

Other diagnostic considerations and algorithms exist, but their availability varies in resource-limited settings. If HIV-infected patients are found to have TB, they should begin TB treatment via Directly Observed Therapy which has been shown to improve the chances for cure compared to self-administered therapy. A widely recommended and used antibiotic regimen for the treatment of TB consists of two months of a combination of rifampicin, isoniazid, pyrazinamide and ethambutol, followed by four months of rifampicin and isoniazid (2RHZE, 4RH); other equally effective regimens exist and are used.

ICAP Experience with TB Screening in Rwanda

Rwanda is one of the countries where ICAP has had the opportunity to implement specific strategies for TB screening in HIV-infected people. In 2003, Rwanda had an estimated tuberculosis disease incidence of 374/100,000, while approximately 190,000 people, or three percent of the adult population, were living with HIV. The National TB Control Program has implemented the WHO DOTS strategy for TB control since 1990. In 2005, the Ministry of Health created a National Policy on TB/HIV Collaborative Activities. The policy advocates free, routine HIV counseling and testing for all TB patients through TB treatment clinics, access to HIV-related services for TB patients with HIV co-infection, and routine, standardized screening for TB in HIV care and treatment facilities. In Gisenyi Province in western Rwanda, ICAP worked with Gisenyi District Hospital (GDH) staff members to integrate TB/HIV activities and adapt the ICAP TB screening questionnaire for use in HIV-infected patients in Rwanda (see Figure 3).

In a pilot program, the screening questionnaire was administered to all in-patients on the internal medicine ward at GDH. As part of routine in-patient care at GDH, all patients without a known HIV status were also offered provider-initiated HIV counseling and testing. Between December 2005 and June 2006, 770 inpatients were screened for TB using the questionnaire. One hundred and sixty-nine screened positive, and of these, 53 were diagnosed with TB following Rwandan national guidelines; of the 53 patients with TB, 39 (74%) were HIV co-infected. Twenty-two percent of all inpatients in that ward with known HIV-infection had TB.

After this pilot phase, the questionnaire was implemented in the GDH outpatient HIV clinic. Between June and July of 2006, 377 patients attending the HIV clinic were screened for TB at their initial or follow-up visit. Eighty patients screened positive by the questionnaire of whom 9 (11%) were diagnosed as having TB. In a new initiative, TB screening is now being extended into the homes of HIV-infected patients diagnosed with TB with a specific focus on finding children who are TB-exposed or have TB disease. This is being started through coordination with community-based TB treatment supporters.

The TB screening questionnaire is an important element in the Rwandan strategy to integrate care for tuberculosis and HIV. In Gisenyi Province, the questionnaire is currently regularly used to screen HIV-infected patients as part of routine HIV care in both inpatients and outpatients. ICAP has supported the Programme National Intégré de lutte contre la Lèpre et la Tuberculose (PNILT) and the Treatment Research Aids Center (TRAC), both part of the Rwandan Ministry of Health, to adapt and implement this questionnaire as a national tool. Preliminary data from 27 HIV care and treatment sites in Rwanda revealed that up to 30% of patients with HIV who are screened for TB at enrollment are TB suspects and at least 30% of those are subsequently diagnosed with TB.

Figure 3. Rwandan National TB screening questionnaire*

1. Has the patient had a cough for > 3 weeks?

2. Has the patient had night sweats for > 3 weeks?

3. Has the patient lost > 3kg in the past 4 months?

4. Has the patient had fever for > 3 weeks?

5. Has the patient had recent contact with another person with active TB?

- If "Yes" to question 1: The patient is a TB suspect, perform sputum collection for acid fast bacilli smear and continue evaluation for TB per the TB control program diagnostic algorithm for pulmonary TB

- If "No" to question 1 but "Yes" to any other question: The patient is a TB suspect, continue evaluation for TB guided by clinical signs and symptoms. Refer to national reference hospital if necessary.

- If "No" to all the questions: The patient is not a TB suspect at this time, stop investigations for TB and repeat screening with questionnaire in 3 to 6 months.

*modified from ICAP questionnaire.

Figure 4. Lessons Learned: The ICAP Experience in Rwanda

- **Government commitment to integrating the interrelated issues of TB and HIV is critical and greatly facilitates efforts to deal with TB/HIV co-infection.** The Rwandan National Policy on TB/HIV Collaborative Activities was part of the foundation on which ICAP and its partners were able to build their response to TB/HIV co-infection in Gisenyi Province.

- **Offering patients with active TB provider-initiated HIV counseling and testing is an important first step in attending to the special needs of people with TB/HIV co-infection.** Encouraging people to ascertain their HIV status can help them gain access to appropriate care and treatment for HIV.

- **A simple screening questionnaire can facilitate the detection of possible active TB cases.** In Rwanda, both doctors and nurses used the screening tool to query patients about active TB symptoms. If a questionnaire is properly designed and straightforward, even non-medical staff members, such as receptionists, might be able to implement the screening process. Screening questionnaires constitute a low-cost, effective way to increase detection of active TB in countries with limited resources, such as Rwanda, and rural areas, such as Gisenyi Province.

Recommendations

In countries where rates of TB/HIV co-infection are high, including many in sub-Saharan Africa, a coordinated approach to diagnosis and treatment of both infections is essential. ICAP's work in Gisenyi Province in Rwanda demonstrated that it is possible to integrate management of tuberculosis and HIV using existing resources, services and infrastructure, even in rural areas with limited resources. Some very specific strategies used in Rwanda could be equally effective in similar settings. These include the following:

1. Offer systematic and regular TB screening to HIV-infected patients. Screening every three to six months of all patients is warranted.

2. Use a TB screening questionnaire with a simple, effective format. A simple format ensures that patients can respond easily to the questions and a wide spectrum of health care personnel can administer the questionnaire. A sample TB screening questionnaire is shown in Figure 5. In areas where technical tools such as chest radiographs are not available or too expensive for most patients, an effective TB screening questionnaire is particularly valuable and can prompt health care providers to consider a patient to be a TB suspect and pursue the use of available diagnostic testing for TB, such as sputum smears.

- After administering the questionnaire, refer patients who screen negative for repeat screening three to six months later. For patients who screen positive, follow national guidelines for the diagnosis of TB.

3. Extend TB screening to the families of HIV-infected patients. Tuberculosis is a contagious disease, and the families of many people living with HIV, particularly young children in the household and other household members living with HIV, are at risk for acquiring latent TB infection and developing TB disease.

4. Introduce tools that collect information on both TB and HIV. Medical records for HIV-infected patients that prompt providers to use questionnaires to screen for TB and to record the results of such screening can help ensure that management of the two infections is genuinely integrated.

5. Institute routine provider-initiated HIV counseling and testing for TB patients as a means of determining which individuals with TB are HIV-infected. TB patients who accept counseling and testing and are found to be HIV-infected will be a better position to be referred to and receive appropriate treatment for both HIV and tuberculosis, as necessary. Patients can always decline to be tested (i.e. "opt-out").

Conclusion

Tuberculosis is the leading cause of death in people living with HIV/AIDS. An integrated approach to the two illnesses is crucial, especially in countries with high prevalence of both TB and HIV. National governments, clinical sites caring for people with HIV and/or TB infection, and international partners can take a number of steps to ensure integration of these services in the interest of persons with both HIV and TB. There is clear evidence, from the documented experience of ICAP and other researchers, that a simple questionnaire can be a highly effective tool in screening HIV-infected patients for possible TB. In the absence of more expensive technical procedures, the use of simple, easy-to-use screening tools becomes especially valuable. This can lead to earlier diagnosis of TB, earlier treatment of TB and a better outcome for the patient with HIV infection. Identification of HIV in patients with TB can enhance their outcomes by providing them with lifesaving interventions such as cotrimoxazole and

Acknowledgement

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More Information on TB/HIV

In addition to the bibliography below, these sources contain further information on TB/HIV co-infection management and care:

Double Scourge: Tuberculosis and HIV Co-infection, by Wafaa El-Sadr. Available at: http://www.tballiance.org/pdf/elsadrv6n4.pdf

TB/HIV Clinical Manual. Available at: http://www.who.int/tb/publications/who_htm_tb_2004_329/en/index.html.

Guidelines for Implementing Collaborative TB and HIV Programme Activities. Available at: http://whqlibdoc.who.int/hq/2003/WHO_CDS_TB_2003.319.pdf.

World Health Organization (WHO) Interim Policy on Collaborative TB/HIV Activities. Available at: http://www.who.int/tb/publications/tbhiv_interim_policy/en/index.html.

WHO Strategic Framework to Reduce the Burden of TB/HIV. Available at: http://www.who.int/tb/publications/who_cds_tb_2002_296/en/index.html.

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Appendix

Figure 5. ICAP Tuberculosis Screening Questionnaire*

	YES	NO
1. Has the individual had a cough for > 2 weeks?	[ ]	[ ]
2. Has the individual had fevers for > 2 weeks?	[ ]	[ ]
3. Has the individual had an observed weight loss > 3 kg in last 4 weeks?	[ ]	[ ]
4. Has the individual had night sweats for > 2 weeks?	[ ]	[ ]
5. Has the patient been in close contact with someone with TB in the past year? (optional)	[ ]	[ ]
6. If done, does the patient have a Tuberculin Skin Test (TST) induration of >5mm? (optional)	[ ]	[ ]

If 'YES' to Question 1, patient is a pulmonary TB suspect, regardless of answers to other questions, begin evaluation for TB.

If 'NO' to Question 1 but 'YES' to any other question, patient is a TB suspect. Begin evaluation for TB.

If 'NO' to all questions, patient is not a TB suspect. Repeat TB screening in 3-6 months time.

* modified from Mohammed et al. IJTLD. 2004

Notes

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